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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,302	10/30/2003	Curt R. Freed	UTC-07994	3925

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Christine A. Lekutis
MEDLEN & CARROLL, LLP
Suite 350
101 Howard Street
San Francisco, CA 94105

EXAMINER	
GAMETT, DANIEL C	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,302	FREED ET AL.	
	Examiner	Art Unit	
	Daniel C. Gamett, PhD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-9 and 11-22* is/are rejected.

7)☒ Claim(s) *3,4, and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-4, 6-19, and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn methods and products wherein human embryonic stems are contact with a solution comprising at least one soluble molecule expressed by fetal striatal cells (claims 1-19) and further comprising at least one soluble molecule expressed by stromal cells in claim 22. The fact that a patent is directed to method entailing use of a compound, rather than to the compound *per se*, does not remove patentee's obligation to provide description of the compound sufficient to distinguish infringing methods from noninfringing methods (University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CAFC 2004)). In this case, the claims are drawn to methods and products that comprise two genera of compounds recited as "at least one soluble molecule expressed by fetal striatal cells" and "at least one soluble molecule expressed by stromal cells". To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the

genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the specification discloses that condition media, and/or undefined substances provided by contact with fetal striatal cells or PA6 stromal cells, and/or GDNF promote differentiation of hES into TH+ neurons. Of these, only GDNF meets the description of "one soluble molecule". Description of a conditioned medium does not provide description of all or any soluble molecules in the medium. No structure or structure/function correlation is provided for the claimed molecule. Even the function of claimed molecule is uncertain; the claims recite that the molecule is contacted with hES in a method for producing TH+ neurons, the molecule is not required to actually do anything.

3. With the exception of GDNF, the skilled artisan cannot envision the detailed chemical structure of the encompassed molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1,2, 6,7,11-15, and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6833269, filed May 31, 2001. Claims 1 and 2 are drawn to a method comprising the steps of: a) providing a human embryonic stem cell line; and b) contacting said embryonic stem cell line with a solution comprising at least one soluble molecule expressed by fetal striatal cells (specifically astrocytes in claim 2), under conditions suitable for producing tyrosine hydroxylase-positive neurons. It is noted that claim 1 does not recite any specific soluble factor, nor does it require coculture of ES cells with fetal striatal cells, or the use of media conditioned by fetal striatal cells. Therefore claims 1 and 2 are anticipated by any instance wherein hES are contacted with a soluble factor that is also expressed by fetal striatal astrocytes. The '269 patent teaches (throughout) derivation of neural cells from human embryonic stem cells. The method for deriving TH+ neurons comprises contacting hES with neurotrophin 3 and BDNF (Table 7, col. 32). Fetal astrocytes express NT-3 and BDNF, as evidenced by Moretto et al., (Journal of Neuropathology and Experimental Neurology, 53(1): 78-85, 1994; see Abstract). Dependent claims 6 and 7 recite a process for producing the "soluble molecule expressed by fetal striatal

cells" of claim 1. Such molecules are known in the art (e.g. NT-3 and BDNF), and recitation of a novel process does not make them patentably distinct. The courts have established that if a claimed product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe,* 227 USPQ 964, 966 (Fed. Cir. 1985); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983).

6. Claims 11-15 are drawn to a cell culture comprising tyrosine-hydroxylase-positive (TH+) neurons derived from human embryonic stem cells. In Claim 11, the culture is derived by a method that is essentially the same as the method of claim 1, and is therefore anticipated by the'269 patent for reasons indicated above. Claims 12-15 recite methods that differ from the methods taught in the prior art. Nevertheless, the product is the same—a cell culture comprising TH+ neurons. The courts have established that if a claimed product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe,* 227 USPQ 964, 966 (Fed. Cir. 1985); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983). The '269 patent teaches use of the cell product for the treatment of Parkinson's disease (column 6, lines 19-32), which further underscores the functional equivalency of the instantly claimed cells and those of the '269 patent by teaching the same intended uses recited in instant claims 14 and 15 and anticipates instant claim 16.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 5, 8, 9, and 16-22 are rejected under rejected under 35 U.S.C. 103(a) as being unpatentable over Kawasaki *et al.*, Neuron, 28:31-40, October 2000. Claim 1 is drawn to a method comprising the steps of: a) providing a human embryonic stem cell line; and b) contacting said embryonic stem cell line with a solution comprising at least one soluble molecule expressed by fetal striatal cells, under conditions suitable for producing tyrosine hydroxylase-positive neurons. Dependent claim 5 indicates that said at least one soluble molecule comprises glial-derived neurotrophic factor. Dependent claim 8 recites contacting said human embryonic stem cell line with stromal cells. It is noted that while claim 5 indicates that fetal striatal cells express GDNF, claim 1 does not require coculture of ES cells with fetal striatal cells or the use of media conditioned by fetal striatal cells. Therefore claim 1 is anticipated by any instance wherein ES are contacted with GDNF. Kawasaki *et al.* teach that coculture with stromal cell line PA6 results in differentiation of ES into dopaminergic neurons (see figure 4). Kawasaki *et al.*, further tested GDNF for possible effects on differentiation induced by the stromal cell line-derived factor (see page 36, final paragraph). Thus, Kawasaki *et al.* contacted ES cells with stromal cells and with GDNF, a soluble molecule expressed by fetal striatal cells, as recited in claims 1,5, and 8 thereby creating the compositions recited in claims 20-22. Kawasaki *et al.*

tested their cell composition in a mouse model of Parkinson's disease as recited in claims 16 and 17. Therefore, the teachings of Kawasaki *et al.* anticipate the limitations of claims 1, 5, 8, 16, 17, and 20-22, with the exception that mouse, not human, ES cells were used. One of skill in the art would be motivated to use human ES cells in order to develop neuronal replacement therapies for Parkinson's disease, as suggested by Kawasaki *et al.* (page 38, left column). Kawasaki *et al.* further indicate that one of skill in the art would expect to use human ES cells with a reasonable expectation of success: "We infer that the same principles should be applicable to human cells, as the early development phase relevant to ES cell differentiation exhibits minimal differences across mammalian species in general. However, minor modifications may be necessary as some properties of human ES cells differ in culture conditions from mouse ones, such as LIF-independent growth" (page 38, left column). Further, enriching the population of TH+ neurons (claim 9), assessing the therapeutic results (claim 18), and use of the method with any stage of Parkinson's disease (claim 19) would be obvious to one of skill in the art.

Conclusion

9. Claims 1,2, 5-9, and 11-22 are rejected.

10. Claims 3,4, and 10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D.,whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG
Art Unit 1647
20 June 2006

DAVID S. ROMEO
PRIMARY EXAMINER